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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/054,354	Applicant(s) LAWTON ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5-9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification Objections

1. The specification is objected to because of the following informalities: *Ehrlichia* is the name of a genus and should be italicized. For example, page 10, line 17 and line 22.

2. The specification is objected to because of the following informalities: The use of trademarks throughout the specification. For example, page 17, line 22. Applicant is asked to review the specification for these type of errors and correction is required.

Claim Objections

3. Claims 4-6 are objected to because of the following informalities: *Ehrlichia* is the name of a genus and should be italicized.

4. Claims 5-6 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 5-6 do not further limit the structure of the product composition and are intended use only and do not limit the structure of the product.

Information Disclosure Statement

5. The form PTO-1449 attached to the information Disclosure statement filed with this application on January 22, 2002 has been detached. The references listed on the information disclosure statement (paper no.5) have been considered. Applicant should submit a replacement PTO-1449 with the reply to this Office action and the PTO-1449 will be signed, dated and returned to applicant for their records.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention a composition and an article of manufacture comprising the isolated polypeptide of SEQ ID No: 1 and variants thereof. The specification states that "variants in which amino acids of the polypeptides of the invention are substituted, deleted or added in any combination are contemplated by the invention". The specification also states " that naturally occurring variants and non-naturally occurring variants are included in the invention and may be

produced by mutagenesis techniques or by direct synthesis" (page 7). Applicant has broadly described the invention as embracing any substitution, insertion or deletion change of amino acids throughout the length of the polypeptide sequence. Variants of SEQ ID No:1 correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found

unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 1 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

7. Claims 1-6 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition of matter and an article of manufacture that comprises an isolated polypeptide shown in SEQ ID No:1, does not reasonably provide enablement for a composition or an article of manufacture that comprises variants of SEQ ID. No:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-6 are directed to a composition of matter and an article of manufacture comprising the isolated polypeptides of SEQ ID NO: 1 and variants thereof.

The specification is enabling only for the polypeptides of SEQ ID NO:1 as disclosed in the specification. The specification states that "variants in which amino acids of the polypeptides of the invention are substituted, deleted or added in any combination are contemplated by the invention". The specification also states " that

naturally occurring variants and non-naturally occurring variants are included in the invention and may be produced by mutagenesis techniques or by direct synthesis" (page 7). The specification teaches that there are many tolerable and conservative amino acid substitutions which can be made that are not critical to protein function (pages 7-9). There is no guidance provided as to which amino acids can be added, deleted or substituted and the polypeptide would retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity/utility requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the

positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polypeptide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modifications, e.g., multiple substitutions. The sequence of some polypeptides is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such polypeptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other antigens having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptides that are variants of SEQ ID NO: 1 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 3 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 3 is indefinite because it recites "a polypeptide shown in SEQ ID No:1". It is unclear as to what the Applicant is referring?

9. Claim 5 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite because it is unclear as to whether the Applicant is claiming a product or process. Clarification is required.

10. Claim 5 is indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 5 is indefinite because it recites "under conditions". It is unclear as to what the Applicant is referring?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3 are rejected under 35 U.S.C. 102(b) as anticipated by Rikihisa et al *(WO 99/13720 published March 25, 1999).*

Claims 1-3 are drawn to a composition of matter and an article of manufacture comprising an isolated polypeptide shown in SEQ ID No:1 or variants thereof.

Rikihisa et al teach diagnostic tools for veterinary and human use which are used for serodiagnosing ehrlichiosis in mammals (see the Abstract). Rikihisa et al teach compositions of matter and articles of manufacture which such as a column, plastic dish, matrix or membrane preferably nitrocellulose containing an isolated outer membrane of *E. chaffeensis or E. canis.* used in a diagnostic method of detecting antibodies to the *E. chaffeensis or E. canis* in a sample of bodily fluid from a patient (page 11). Which meets the claim limitation that "the article of manufacture comprises packaging material and contained within the packaging material the polypeptide shown in SEQ ID NO:1". Rikihisa et al teach the isolated polypeptide shown in SEQ ID NO:1, (see Figure 21B). Therefore, the composition of matter and article of manufacture of Rikihisa et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's composition of matter and article of manufacture with the composition of matter and article of manufacture of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the composition of matter and article of manufacture of the prior art does not possess the same material structural and functional characteristics of the claimed composition of matter and article of manufacture). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rikihisa et al *(WO 99/13720 published March 25, 1999)* in view of *Waner et al (J Ve. Diagn Invest. 12:240-244, 2000).*

Claims 1-6 are drawn to a composition of matter and an article of manufacture comprising an isolated polypeptide shown in SEQ ID No:1 or variants thereof wherein

the article of manufacture comprises a label that indicates that the polypeptide can be used for the identification of *Ehrlichia* infection in a mammal.

Rikihisa et al teach diagnostic tools for veterinary and human use which are used for serodiagnosing ehrlichiosis in mammals (see the Abstract). Rikihisa et al teach compositions of matter and articles of manufacture which such as a column, plastic dish, matrix or membrane preferably nitrocellulose containing an isolated outer membrane of *E. chaffeensis or E. canis.* used in a diagnostic method of detecting antibodies to the *E. chaffeensis or E. canis* in a sample of bodily fluid from a patient (page 11). Rikihisa et al teach the isolated polypeptide shown in SEQ ID NO:1, (see Figure 21B).

Rikihisa et al do not teach the use of a label indicates that the polypeptide can be used for the identification of *Ehrlichia* infection in a mammal.

Waner et al teaches a label that indicates the use of the composition of matter or the article of manufacture (page 241, Figure 1).

It would be *prima facie* obvious at the time the invention was made to add label as taught by Waner et al to the composition of matter or article of manufacture of Rikihisa et al because it is well known in the art to include packing material and a label to indicate the intended use of the composition of matter or article of manufacture.

The printed matter on a label or package insert does not lend patentable weight as a limitation of the claimed product, composition, or article of manufacture, absent a functional relationship between the label or package insert and the product, composition of matter or article of manufacture. See In re Haller 73 USPQ 403 (CCPA 1947), where

it is held that application of printed matter to old article cannot render the article patentable. In the opinion text of In re Haller, it is stated that: Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned...In accordance with the patent statutes, an article or composition of matter, in order to patentable, must not only be useful and involve invention, but must also be *new.* If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it is intended. The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statues make no provision for patenting of an article or composition which is not, in and of itself, new.

Also see In re Venezia 189 USPQ 49 (CCPA 1976), where kits are drawn to the structural attributes of interrelated component parts and not to activities that may or may not occur. Further, In re Miller 164 USPQ 46 (CCPA 1969) and In re Gulak (CA FC)217 USPQ 401 relate to a mathematical device and to a measuring cup respectively. In each of these cases, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed articles. The polypeptides of the claimed articles remain fully functional absent the labeling or printed instructions for use.

It is further noted that the written material in the instructions is not considered to be within the statutory classes and does not carry patentable weight. See MPEP 706.03(a).

Thus the instructions for use included in composition of matter and article of manufacture constitute an "intended use" for that composition of matter or article of manufacture. Intended use does not impart patentable weight to a product. See MPEP 2111.03: Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey, 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459 (CCPA 1963)

In the instant case, the claims are drawn to a composition of matter and an article of manufacture which comprises an isolated polypeptide shown in SEQ ID NO:1, and a label that indicates the use of the composition of matter or article of manufacture. The intended use which is recited on the label or package insert lacks a function relationship to the polypeptide because the insert or label does not physically or chemically affect the chemical nature of the polypeptide within the composition of matter or article of manufacture, and furthermore, the polypeptide can still be used by the skilled artisan for other purposes. Therefore the polypeptide which are comprised within

the composition of matter and the article of manufacture are unpatentable over the prior art polypeptide, because they function equally effectively with or without the labeling, and accordingly *no functional relationship exists between the instructions for use and the polypeptide.*

Thus the claims are addressed as being drawn to a composition of matter and an article of manufacture comprising an polypeptide and a label that indicates that the polypeptide can be used for the identification of *Ehrlichia* infection in a mammal, the instructions on the label bearing no patentable weight with regard to double patenting, 102, and 103 rejections.

Status of Claims

13. No claims are allowed.

Conclusion

14. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909

Vanessa L. Ford
Biotechnology Patent Examiner
September 9, 2003

PATRICIA A. DUFFY
PRIMARY EXAMINER